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EXAMINER

KANTAMNENI, SHOBHA

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/789,814	Applicant(s) BABISH ET AL.	
	Examiner Shobha Kantamneni	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) NONE is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-7 are pending and examined herein.

Claim Objections

Claims 5, 6 are objected to because of the following informalities: Claims 5, and 6 should depend on claim 4 and not on claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing inflammation by inhibiting COX-2 synthesis of PGE2, **does not reasonably provide enablement for reducing any** inflammation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that **any** inflammation can be treatable by using compounds described in the method claims 4-7.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without **undue experimentation**. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a

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disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of reducing inflammation by administering compounds such as reduced isoalpha acid and isoalpha acid isolated from hops. The nature of the invention is complex in that it encompasses reducing **any** inflammation.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a method of reducing **any inflammation** by administering compounds having formula shown in claim 7 or a reduced isoalpha acid and isoalpha acid isolated from hops. What's more, the scope of the compounds claimed to be useful for the method of reducing inflammation is extremely broad. There are a number of possible compounds of formula shown in claim 7 for the treatment claimed.

(3). Guidance of the Specification:

All of the guidance provided by the specification is directed toward the method of reducing inflammation by inhibiting COX-2 synthesis of PGE2 by administering

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reduced alpha acid and isoalpha acid isolated from hops. Thus the guidance given by the specification as to how one would administer the claimed compounds to a subject in order to reduce inflammation is limited.

(4). Working Examples:

Applicant provides examples of inhibition of COX-2 syntheses of PGE₂, by using reduced isoalpha acid and isoalpha acid isolated from hops in stimulated and nonstimulated murine macrophages. See page 21, EXAMPLE 1.

(5). State of the Art:

While the state of the art is relatively high with regard to reducing specific type of inflammation, the state of the art with regard to reducing **any** inflammation broadly is underdeveloped. In particular, there is no known anti-inflammatory agent which is effective against all types of inflammations. Merck Manual, Fifteenth Edition (pages 2246-2260, 1239-1261, and 2497-2503) clearly teaches that there are wide variety of inflammatory disorders and are treated using different anti-inflammatory drugs, none are effective against reducing all types of inflammation (pages 2246-2260, 1239-1261, and 2497-2503) because "inflammatory disorder" will respond differently and only some aspects of inflammation may respond to any given drug. There are compounds that treat a range of inflammation, but no one has ever been able to figure out how to get a compound to be effective against reducing **any** inflammation. Thus, the existence of such a "silver bullet" is contrary to our present understanding. This is true in part because inflammation arise from a wide variety of sources, such as viruses (e.g. rubella, mums), bacteria (infectious arthritis), environmental and genetic

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factors, and a wide variety of failures of the body's cell growth regulatory mechanisms. Also different types of inflammation affect different parts of body and are treated differently, for example dermatological disorders such contact dermatitis which is an inflammation of the skin may be caused by a chemical irritant or may be a Type IV delayed hypersensitivity reaction, and is treated using an oral corticosteroid, whereas rheumatoid arthritis an inflammatory disorder is treated using Nonsteroidal anti-inflammataory drugs (NSAIDS). There is no such thing as a treatment of these generally because of their diversity. Thus, it is beyond the skill of a **person** today to get an agent to be effective against reducing **any** inflammation generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

(6). Predictability of the Art:

The invention is directed to a method of reducing **any** inflammation in general. It is well established that "the scope of enablement various inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970). Inflammations are especially unpredictable due to their complex nature. Please refer to the discussion of Merck Manual and the state of the art in (5) that shows the different treatments of inflammatory disorders. The treatment of one type of inflammation could not be necessarily the same for the other type.

(7). The Quantitv of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of compounds, an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for reducing inflammation. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding reducing inflammation with any compound represented by formula in claim 7, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of inflammation because, as described in Merck Manual there is no known drug effective for reducing all types of inflammation. Therefore, it would require **undue, unpredictable experimentation** to practice the claimed invention to reduce inflammation by administering a combination of compounds.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

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Therefore, a method for reducing **any inflammation broadly** by administering the various combination of compounds such as reduced isoalpa and isoalpa isolated from hops of the claims is not considered to be enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrases “reduced isoalpa acid” and “isoalpa acid” renders the claim indefinite, as it is not clear what other compounds this phrase encompasses, since one of ordinary skill in the art would not ascertain the metes and bounds as to “reduced isoalpa acid” and “isoalpa acid”.

Note: Applicants insertion of chemical structures for reduced isoalpa acid and isoalpa acid will be favorably considered.

Claims 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrases “wherein R is alkyl” renders the claim indefinite, as it is not clear what other compounds this phrase encompasses, since one of ordinary skill in the art would not ascertain the metes and bounds as to “wherein R is alkyl”.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhrts (US 2004/0137096, PTO-892).

The instant invention is drawn to composition comprising a reduced isoalpha acid and isoalpha acid isolated from hops, and a method of reducing inflammation by administering said composition.

Kuhrts teaches pharmaceutical compositions comprising hops extract consisting of iso-alpha acids such as iso-humulone, iso-cohumulone, iso-adhumulone, dihydro-iso-humulone, di-hydroiso-adhumulone of the instant formula (Genus A), and combinations thereof. See page 4, paragraph [0027]; page [0031]; page 5, paragraph [0034], Example 1, wherein 3 % of Iso-alpha acids are present in the Hops extract; page 6, claims 1-5, 21-25.

Furthermore Kuhrts teaches the same method of reducing inflammation as instantly claimed, comprising administering Hops extract consisting of Iso-alpha acids and reduced iso-alpha acids such as iso-humulone, iso-cohumolone, iso-adhumolone, dihydro-iso-humolone, di-hydroiso-adhumolone. See page 5, paragraphs [0035]-[0038].

Kuhrts does not expressly teach the ratio of reduced isoalpa acid : isoalpa acid as about 3:1 to about 1:10, in the composition.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of the reduced isoalpa acid : isoalpa acid employed in the composition of Kuhrts, to obtain a desired effect such as reducing inflammation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of Iso-alpha acid and reduced isoalpa acid employed in the pharmaceutical compositions for methods of reducing inflammation in which the ratio of isoalpa acid : isoalpa acid is about 3:1 to about 1:10, since the optimization of effective amounts of known agents to be administered , is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tobe (US 5,604,263, PTO-892).

The instant invention is drawn to a composition comprising a reduced isoalpa acid and isoalpa acid isolated from hops, and a method of reducing inflammation by administering said composition.

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Tobe teaches a method of treating inflammatory disorder osteoporosis, comprising administering a pharmaceutical composition comprising an effective amount of one or more compounds selected from alpha acids, isoalpha acids and derivatives contained in hop extract such as isohumulone, isocohumulone, and isoadhumulone of the instant claims. See abstract; column 2, structures (IV) to (VI), lines 64-67; column 8, claim 1-4.

Tobe does not expressly teach the ratio of the two compounds as about 10:1 to about 1:10 in the composition.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of the reduced isoalpha acid : isoalpha acid employed in the composition of Tobe, to treat osteoporosis.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of compounds such as isohumulone, isocohumulone, and isoadhumulone employed in the pharmaceutical compositions for methods of reducing inflammation in which the ratio of two compounds is about 10:1 to about 1:10, since the optimization of effective amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhrts (US 2002/0086070, PTO-892).

Kuhrts teaches a pharmaceutical composition comprising hops (*Humulus lupulus* L) extract for treating inflammatory disorders such as osteoarthritis, rheumatoid arthritis. See page 2, paragraphs [0014], and [0016]. Kuhrts further teaches liquid carbon dioxide under supercritical conditions is a preferred extraction technique to obtain the components from the hops. See page 2, paragraphs [0016]- [0018]; page 6, claims 1-14.

Since Kuhrts teaches the same extract i.e., derived from hops obtained by the same process as recited by the instant claims and specification, Kuhrts hops extract will contain the components isoalpa acids and reduced isoalpa acids as recited by instant claims.

Kuhrts does not expressly teach the ratio of reduced isoalpa acid : isoalpa acid as about 3:1 to about 1:10 in the composition.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of the reduced isoalpa acid : isoalpa acid employed in the composition of Kuhrts, to obtain a desired effect such as reducing inflammation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of Iso-alpha acid and reduced isoalpa acid employed in the pharmaceutical compositions for methods of reducing inflammation in which the ratio of isoalpa acid : isoalpa

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acid is about 3:1 to about 1:10, since the optimization of effective amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Note: The ratio of RIAA to IAA of the instant claims such as 3:1 to 1:10; and 10:1 to 1:10 is broad and might read on the ratio of the prior art composition, or read on the naturally occurring ratio of the two compounds in the natural product (hops extract).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-115 of

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copending Application No. 10/464410. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claims overlaps with the stated claims of 10/464410. Note that "A composition comprising, as a first component, a fraction derived from hops" in the copending application implies that the composition would contain isoalpa and reduced isoalpa acid . The claimed composition, and method of reducing inflammation are within the scope of the claims of the copending Application 10/464410. It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as effective amounts of the reduced isoalpa acid : isoalpa acid, to treat inflammation.

Claims 4-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-34 of copending Application No. 10/464834. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claims overlaps with the stated claims of 10/464834. Note that, "comprising a fraction isolated or derived from hops" in the copending application implies that the pharmaceutical composition would contain isoalpa and reduced isoalpa acid. The claimed method of reducing inflammation is within the scope of the claims of the copending Application 10/464834. It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as effective amounts of the

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reduced isoalpha acid : isoalpha acid, to obtain a desired effect such as reducing inflammation.

Claims 1-3 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/689856, and over claims 1-6 of copending Application 10/774048. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claims overlaps with the stated claims of 10/689856. Note that, "A composition comprising as a first component, a fraction isolated or derived from hops" in the copending applications implies that the pharmaceutical composition would contain isoalpha and reduced isoalpha acid. The claimed composition is within the scope of the claims of the copending Application 10/689856, and 10/774048. It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as effective amounts of the reduced isoalpha acid : isoalpha acid, to obtain a desired effect.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

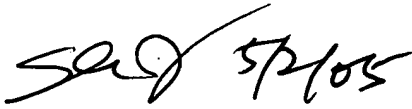
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-5pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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